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## Pregnanolone and 20 -hydroxypregn-4-en-3-one (20 -OH-P) in prolonging gestation in the rat

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# Pregnanolone and 20 -hydroxypregn-4-en-3-one (20 -OH-P) in prolonging gestation in the rat<sup>\*</sup>

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## Abstract

The comparative effectiveness of subcutaneous administration of 20p-OH-P, pregnanolone and progesterone in oil to prolong gestation in rats was determined. As a result it was found that, while progesterone was shown to have activity, pregnanolone and 20j1-OH-P were ineffective in doses of 5 mg per day.

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## **PREGNANOLONE AND 20 $\beta$ -HYDROXYPREGN-4-EN-3-ONE (20 $\beta$ -OH-P) IN PROLONGING GESTATION IN THE RAT**

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Pregnanolone and 20 $\beta$ -hydroxypregn-4-en-3-one (20 $\beta$ -OH-P) were reported to possess a potent depressant effect on smooth muscle motility. According to GYERMEK (1) the former compound was considered to be 4 times as potent as progesterone in its inhibitory effect on isolated rat uterine motility, and recently YOSHIDA *et al.* (2) reported that the latter steroid inhibited isolated rabbit intestinal motility 2-5 times as much as progesterone and had a similar potency on isolated human gestational myometrium. Both steroids are naturally occurring metabolites of progesterone, and 20 $\beta$ -OH-P has been found to possess biological activity in progestational assays (3).

In view of the pronounced inhibitory effect on smooth muscle and a little progestational activity, it was thought that pregnanolone and 20 $\beta$ -OH-P would probably have a potent activity to delay the initiation of parturition. For this reason, a study was carried out to see whether or not these two compounds have some influences on prolonging gestation in rats by comparing with that of progesterone.

### **MATERIALS**

Virgin female rats weighing 180-250 g were kept in temperature-regulated quarters (19-24°C) with free access to food and water. Vaginal smears were examined each morning and pregnancy was diagnosed by the detection of sperm in the vaginal smear, and the day of detection was taken as day zero of pregnancy. Light was controlled, providing 13-14 hr of light and 10-11 hr of dark. Animals were injected subcutaneously at 9 A.M. from gestation day 19 to 22 with 5 mg pregnanolone (Teikoku Zoki), 5 mg 20 $\beta$ -OH-P (Teikoku Zoki) or 5 mg, 3 mg progesterone (Nihon Schering). Ten mg of the hormone were dissolved in 1-ml oily vehicle. All fetuses were collected from each mother and weighed to milligrams.

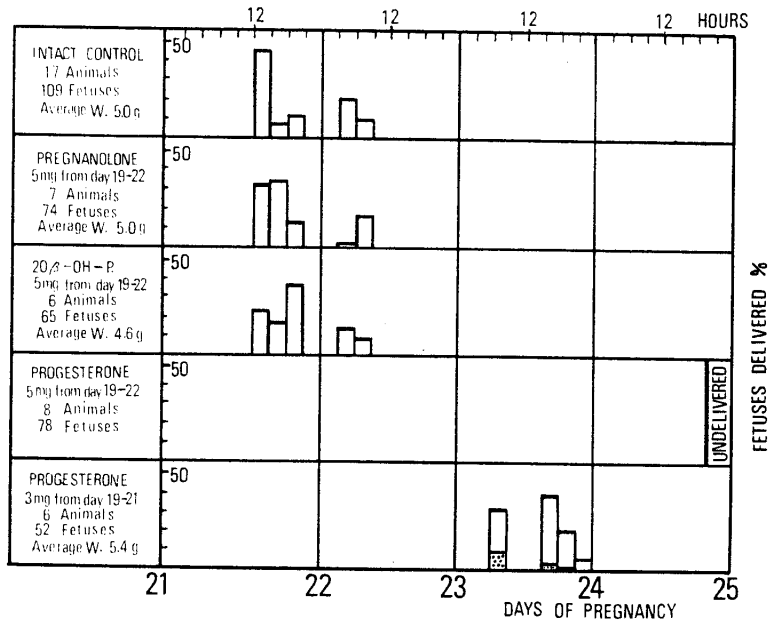


Table 1. Influences of steroid hormones on parturition delay. Bars indicate percentages of fetuses delivered during each 3 hours in each group. Dotted bars: Still-born fetuses.



Fig. 1 A mother injected with 5 mg progesterone per day died with young in uterus and vagina during prolonged and arrested labour. The arrow indicates a fetus.

## RESULTS

At daily dose of 3 mg for three days the ability of progesterone in delaying the parturition is clearly seen (Table 1) and moreover in some rats prolonged and difficult parturition was observed. Eight rats administered with daily dose of 5 mg of progesterone did not parturite till day 25. On the twenty-fifth day 3 rats delivered only 9 dead litters and prolonged and difficult parturition was observed. Two of these rats were dead after delivering a small fraction of their litters (Fig. 1). Other 3 rats did not deliver and were emaciated, dead on 26th or 27th day. At autopsy on the remaining two rats on day 25 all fetuses were dead in uterus. In contrast, it is apparent that pregnanolone and 20 $\beta$ -OH-P, at a dose of 5 mg, were ineffective to prolong the gestation. While these results do not necessarily establish that pregnanolone or 20 $\beta$ -OH-P lacks activity in prolonging gestation, despite its inhibitory activity 4-fold potent on smooth muscle when compared to progesterone and some hormonal properties akin to those of progesterone, these compounds are less potent than progesterone in delaying parturition.

## SUMMARY

The comparative effectiveness of subcutaneous administration of 20 $\beta$ -OH-P, pregnanolone and progesterone in oil to prolong gestation in rats was determined. As a result it was found that, while progesterone was shown to have activity, pregnanolone and 20 $\beta$ -OH-P were ineffective in doses of 5 mg per day.

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